EPA HPV Challenge
Color Former Category Test Plan

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The Color Former Category

Color Former Name	Chemical Name	C.A.S. Number
Black XV	Spiro[isobenzofuran-1(3H),9'-[9H]xanthene]-3-one, 6'-(diethylamino)-3'-methyl-2'-(2,4-dimethylphenylamino)-	36431-22-8
N-102	Spiro[isobenzofuran-1(3H),9'-[9H]xanthen]-3-one, 6'-(diethylamino)-3'-methyl-2'-(phenylamino)-	29512-49-0
ODB-2	Spiro[isobenzofuran-1(3H),9'-[9H]xanthen]-3-one, 6'-(dibutylamino)-3'-methyl-2'-(phenylamino)-	89331-94-2

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Category Definition

1. Identification of Category Members

The EPA High Production Volume (HPV) Challenge identified the following chemical as a high production volume chemical:

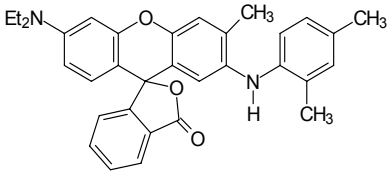
Color Former Name	Chemical Name	C.A.S. Number
Black XV	Spiro[isobenzofuran-1(3H),9'-[9H]xanthene]-3-one, 6'-(diethylamino)-3'-methyl-2'-(2,4-dimethylphenylamino)-	36431-22-8

The EPA guidance document on the development of chemical categories defines a category as “a group of chemicals whose physicochemical and toxicological properties are likely to be similar or follow a regular pattern as a result of structural similarity. The similarity may be based on a common functional group.”

The following two chemicals are very similar to Black XV in molecular structure:

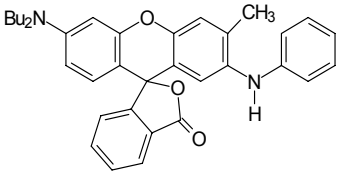
Color Former Name	Chemical Name	C.A.S. Number
N-102	Spiro[isobenzofuran-1(3H),9'-[9H]xanthen]-3-one, 6'-(diethylamino)-3'-methyl-2'-(phenylamino)-	29512-49-0
ODB-2	Spiro[isobenzofuran-1(3H),9'-[9H]xanthen]-3-one, 6'-(dibutylamino)-3'-methyl-2'-(phenylamino)-	89331-94-2

These color formers are not identified by the EPA as HPV chemicals, but their structures and their physiochemical and toxicological properties are so similar that they are being included with Black XV in the color former category. The chemical structure diagrams of these three color formers are shown below.



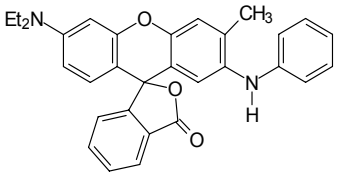
BLACK XV

Formula: $C_{33}H_{32}N_2O_3$
M.W.: 504



ODB-2

Formula: $C_{35}H_{36}N_2O_3$
MW: 532



N102

Formula: $C_{31}H_{28}N_2O_3$
MW: 476

2. Category Analysis

All the color former category members have closely related chemical structures. All of the color formers in this category are flourans with the only differences in the stuctures being the functional group on the nitrogen and the functional groups on the benzene ring attached to the other nitrogen. Black XV and N-102 use the same ethyl group attached to one nitrogen. The difference between them is that Black XV has two methyl groups attached to the benzene ring on the other nitrogen where N-102 has none. ODB -2 is basically the same as N-102, except the ethyl group attached to the nitrogen is replaced with a butyl group.

3. Test Plan Matrix

The color former category test plan matrix that is shown in Table 1 was developed after a review of the existing data available. The matrix is arranged by category members in columns and the screening data endpoints in rows. The table indicates how data are provided for each endpoint.

4. Test Plan Rationale

For each of the screening data endpoints, including physical and chemical data, environmental fate and pathways, ecotoxicity, and toxicologoical data, the rationale for using the category approach is included in the following discussion.

Table 1: Test Plan Matrix for the Color Former Category

Screening Endpoints	Black XV (36431-22-8)	N-102 (29512-49-0)	ODB-2 (89331-94-2)
Physical and Chemical Data			
Melting Point	A	A	A
Boiling Point	NA	NA	NA
Density (Specific Gravity)	A	A	A
Vapor Pressure	C	C	A
Partition Coefficient (n-Octanol/Water)	A	A	A
Water Solubility	A	A	A
pH Value and pKa Value	A	A	A
Environmental Fate and Pathways			
Photodegradation	A	A	A
Stability in Water (Hydrolysis)	A	A	A
Transportation and Distribution between Environmental Compartments	A	A	A
Biodegradation	A	A	A
Ecotoxicity			
Acute Toxicity to Fish	A	A	A
Acute Toxicity to Aquatic Invertebrates	A	A	A
Toxicity to Aquatic Plants (e.g. Algae)	A	A	A
Toxicological Data			
Acute Oral Toxicity	A	A	A
Acute Dermal Toxicity	A	A	A
Repeated Dose Toxicity	C	C	A
Gene mutation	A	A	A
Genetic Toxicity – Chromosomal Aberrations	A	A	A
Toxicity to Reproduction	C	C	A
Developmental Toxicity/Teratogenicity	C	C	A^1

Key: A = Endpoint fulfilled with data
A^1 = Endpoint fulfilled by Toxicity to Reproduction Test data
C = Endpoint fulfilled by other category members data
NA = Test not applicable

4.1 Physical and Chemcial Data

Listed in Table 2 are the values for the physical and chemical data endpoints for the color former category. All of the data listed can be found in the robust summaries for the color former category. The boiling points were not measured because the three color formers in this color former category are solids at room temperature and melt at temperatures above 168°C. No boiling point data has been generated for these color formers. The vapor pressure measured for ODB-2 is very low, as it is a solid; the other color formers in the category would have similar vapor pressures. The water solubility of each color former was measured and found to be very similar. Because the pKa value could not be calculated due to limited solubility for ODB-2, the other color formers in the category would have similar results because of limited solubility. No further physical and chemical tests are planned for the color former category.

Table 2: Physical and Chemical Data

Screening Endpoints	Black XV (36431-22-8)	N-102 (29512-49-0)	ODB-2 (89331-94-2)
Physical and Chemical Data			
Melting Point	168ºC	195ºC	181.5 – 185.0°C
Boiling Point	NA	NA	NA
Density (Specific Gravity)	1.19 g/ml	1.19 g/ml	1.19 g/ml
Vapor Pressure			< 2.6 x 10^{-4} Pa at 25°C
Partition Coefficient (n-Octanol/Water)	Log P_{ow} = 6.5 at 25ºC	Log P_{ow} = 6.2 at 20.5ºC	Log P_{ow} > 4.66 at 20ºC
Water Solubility	0.0405 mg/L at 25ºC	0.0202 mg/L at 20ºC	0.02122 mg/L at 20ºC
pH Value and pKa Value			Not soluble in water enough to perform the test

4.2 Environmental Fate and Pathways

Listed in Table 3 are the values for the environmental fate and pathway endpoints for the color former category. All of the data listed can be found in the robust summaries for the color former category. The photodegradation and hydrolysis endpoints for Black XV, N-102, and ODB-2 were estimated with the EPA model, EPIWin. Because the color formers are solids, the photodegradation pathway is not a very likely scenario for degradation. Very little of the color formers dissolve in water so hydrolysis is also not a very likely route of degradation. The lower half-life for ODB-2 in hydrolysis may be due to using the estimated Log K_{ow} result instead of measured values used in the model for Black XV and N-102. The measured Log K_{ow} for ODB-2 is listed as greater than 4.66 and was not used in the model. The most likely route is adsorption to the soil and biodegradation. The biodegradation results from testing each color former in the category shows that they are all very similar in that they are not readily biodegradable.

Another test that confirmed the information from the modeling is the adsorption/desorption to soil on ODB-2. ODB-2 was strongly absorbed on to the soils tested, and it did not readily desorb from the soils. This result is consistent with the EPIWin modeling information. All the endpoints have adequate data, so no further environmental fate and pathways tests or estimations are planned for the color former category.

Table 3: Environmental Fate and Pathways

Screening Endpoints	Black XV (36431-22-8)	N-102 (29512-49-0)	ODB-2 (89331-94-2)
Environmental Fate and Pathways			
Photodegradation	EPIWin Model Half-life ($t^{1/2}$) = 0.05 days	EPIWin Model Half-life ($t^{1/2}$) = 0.05 days	EPIWin Model Half-life ($t^{1/2}$) = 0.05 days
Stability in Water (Hydrolysis)	EPIWin Model Half-life ($t^{1/2}$) = 150 days	EPIWin Model Half-life ($t^{1/2}$) = 150 days	EPIWin Model Half-life ($t^{1/2}$) = 60 days
Transportation and Distribution between Environmental Compartments	EPIWin Model Air: 0.01% Water:1.74% Soil: 36.6% Sediment: 61.7% Persistence: 225 days	EPIWin Model Air: 0.01% Water:2.07% Soil: 42.3% Sediment: 55.6% Persistence: 232 days	EPIWin Model Air: 0.02% Water:2.39% Soil: 28.7% Sediment: 68.9% Persistence: 106 days
Biodegradation	2% (28 days)	4% (28 days)	5% (28 days)

4.4 Ecotoxicity

Listed in Table 4 are the values for the ecotoxicity endpoints for the color former category. All of the data listed can be found in the robust summaries for the color former category. The data provided is consistent between the color formers in that they are not toxic to fish within their solubility range and are not inhibitory to alga growth within their solubility range. Some further tests that were completed on ODB-2 include a prolonged toxicity study on rainbow trout, bioaccumulation in rainbow trout, a toxicity study of OBD-2 on earthworms, and a toxicity test of ODB-2 on the growth of higher plants. These tests also show that there were no adverse effects at the dose levels given. All of the endpoints have adequate data, so no further ecotoxicity testing is planned for the color former category.

Table 4: Ecotoxicity

Screening Endpoints	Black XV (36431-22-8)	N-102 (29512-49-0)	ODB-2 (89331-94-2)
Ecotoxicity			
Acute Toxicity to Fish	96 h LC_{50} > 7.6 mg/L	96 h LC_{50} > 10 mg/L	96 h LC_{50} > 1.0 mg/L
Acute Toxicity to Aquatic Invertebrates	No toxicity within aqueous solubility	No toxicity within aqueous solubility	No toxicity within aqueous solubility
Toxicity to Aquatic Plants (e.g. Algae)	72 h EC_{50} > 3.1 mg/L, Not inhibitory to growth within aqueous solubility	72 h EC_{50} > 33.7 mg/L, Not inhibitory to growth within aqueous solubility	72 h EC_{50} > 0.76 mg/L, Not inhibitory to growth within aqueous solubility

4.5 Toxicological Data

Listed in Table 5 are the values for the toxicological endpoints for the color former category. All of the data listed can be found in the robust summaries for the color former category. The data provided is consistent between the color formers in that the oral toxicity was found to be greater than the highest does level, and the dermal toxicity was greater than the highest dose level. In addition to dermal toxicity, each color former was tested for skin irritation (rabbit), eye irritation (rabbit), and skin sensitization (guinea pig). All of these tests show the color formers in this category show little or no irritation to the skin or eyes or sensitization to the skin. The repeated dose result for ODB-2 is consistent with this pattern of the color formers in this category, which shows no toxicity at the greatest dose tested. All of the gene mutation tests on each color former and the chromosomal aberration tests on each color former were negative. The reproduction test on ODB-2 was based on the OECD Method 415, which showed no signs of toxicity. The reproduction test was carried on for 10 weeks prior to mating and carried through to 21 days post partum. Based on the results of this test no further developmental tests were conducted. The color formers in this category show a clear pattern of low toxicological concern, so no further toxicological testing is planned for the color former category.

Table 5: Toxicological Data

Screening Endpoints	Black XV (36431-22-8)	N-102 (29512-49-0)	ODB-2 (89331-94-2)
Toxicological Data			
Acute Oral Toxicity	LD_{50} > 10.0 g/kg	LD_{50} > 2.0 g/kg	LD_{50} > 5.0 g/kg
Acute Dermal Toxicity	LD_{50} > 2.0 g/kg		LD_{50} > 2.0 g/kg
Repeated Dose Toxicity			NOEL > 1000 mg/kg/day
Gene mutation	Negative	Negative	Negative
Genetic Toxicity – Chromosomal Aberrations	Negative	Negative	Negative
Toxicity to Reproduction			NOEL = 1000 mg/kg/day
Developmental Toxicity/Teratogenicity			See above result

5. Test Plan Conclusion

All three of the color former category members have closely related chemical structures. All of the color formers in this category are flourans with the only differences in the stuctures being the functional group on the nitrogen and the functional groups on the benzene ring attached to the other nitrogen. All of the data from the robust summaries for the color former category show a similar pattern of physical and chemical properties, and a similar pattern of little or no adverse effects from environmental fate data, ecotoxicity data, and toxicological data.

The data provided in the robust summaries show a pattern that is consistent with the close molecular structure of the color formers in this category. The data help confirm the validity of the category. No further new testing is planned for the color former category.